

## REMARKS

Claims 47-49, and 54-66 are pending in the instant application. Claims 47, 54, 59 and 62 have been amended herein. The claims as amended are fully supported by the as-filed specification. Accordingly, no new matter has been added by these amendments.

### I. Withdrawn Objections/Rejections

Applicants note that the Examiner has withdrawn all objections to the specification. In addition, the Examiner has withdrawn all rejections and objections to claims 50-53, which Applicants cancelled in the previous Response and Amendment mailed May 22, 2003. The Examiner has also withdrawn the rejections of claims 47-53 under 35 U.S.C. § 112, second paragraph (labeled A-D in the January 29, 2003 Office Action (Paper No. 18)). The rejections under 35 U.S.C. § 103(a) in view of the Marshall, Hesselberth, Cox and Scaringe references have also been withdrawn.

### II. Claim rejections under 35 U.S.C. § 102

#### Marshall

The Examiner has rejected claims 47, 49, 54-59 and 61-66 under 35 U.S.C. §102(a) as being anticipated by Marshall *et al.*, *Nature Structural Biology*, vol. 6(11):992-94 (1999) (“Marshall”). According to the Examiner, independent claims 47, 59 and 66 are anticipated, because Marshall discloses “aptazyme chips” in which different ribozyme ligases are immobilized on beads in wells to monitor the presence and concentration of different metabolites or proteins. (Office Action, p. 3). In addition, the Examiner has asserted that dependent claims 49, 54-58 and 61-65 are also anticipated, because Marshall discloses the use of “amplification” of the signal produced, “fluorescently tagged substrates”, “beads in wells on a multi-well plate”, different aptazymes being immobilized in different wells, and detection of metabolites and proteins. (Office Action, p. 4).

Applicants traverse. Applicants submit herewith a Declaration of the named inventors of the instant application, Dr. Andrew D. Ellington, Dr. Kristin Thompson (formerly Dr. Kristin Marshall, the lead author of the Marshall reference), and Dr. Michael Robertson under 37 C.F.R.

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§1.131 (“the Declaration”). The Declaration demonstrates that the Marshall reference is unavailable as prior art in the instant application. The Marshall reference describes the work of Dr. Ellington and Dr. Thompson, two of the named inventors in the instant application, as well as the named authors of the Marshall reference. As demonstrated in ¶¶4-10 of the Declaration, the Marshall publication refers to work that ultimately generated the aptamer constructs, arrays, and methods of the claimed invention. In light of the fact that the Marshall reference represents the scientific publication of this work, the methods recited by pending claims 47, 49, 54-59 and 61-66 were necessarily invented before the publication date of the Marshall reference. (See Declaration, ¶10). Thus, the inventions claimed in the instant application were not known or used by others in this country, or described in a printed publication before Applicants invented them. Accordingly, Marshall is not available as prior art under 35 U.S.C. §102(a), and Applicants request that the Examiner withdraw this rejection.

Hesselberth

Claims 47, 49, 54, 58, 61-62, 65-66 have also been rejected under 35 U.S.C. §102(a) as being anticipated by Hesselberth *et al.*, *Reviews in Molecular Biotechnology*, vol. 74:15-25 (2000) (“Hesselberth”). With regard to claim 47, the Examiner has asserted that Hesselberth discloses methods for the “high-throughput construction of chips to sense proteomes and metabolomes.” (Office Action, p. 7). The Examiner has concluded that claim 49 is anticipated by Hesselberth, because this reference discloses ribozymes having appended tags that can be “preferentially amplified.” (Office Action, p. 8). In addition, the Examiner has asserted that dependent claims 49, 54-58 and 61-65 are also anticipated, because Marshall discloses the use of “amplification” of the signal produced, “fluorescently tagged substrates”, “beads in wells on a multi-well plate”, different aptazymes being immobilized in different wells, and detection of metabolites and proteins. (Office Action, p. 8).

Applicants traverse. The Declaration submitted herewith also demonstrates that the Hesselberth reference is unavailable as prior art in the instant application. The Hesselberth reference describes the work of Dr. Ellington and Dr. Robertson, two of the named inventors in the instant application, as well as two of the named authors of the Hesselberth reference. As demonstrated in ¶¶11-16 of the Declaration, the Hesselberth reference presents work that

ultimately produced the aptamer constructs, arrays, and methods claimed in the instant application. As the Hesselberth reference represents the scientific publication of this work, the methods recited by pending claims 47, 49, 54, 58, 61-62 and 65-66 were necessarily invented before the publication date of the Hesselberth reference. (See Declaration, ¶16). Thus, the inventions claimed in the instant application were not known or used by others in this country, nor were the methods recited by the instant application described in a printed publication before Applicants invented them. Accordingly, Hesselberth is not available as prior art under 35 U.S.C. §102(a), and Applicants request that the Examiner withdraw this rejection.

### **III. Claim rejections under 35 U.S.C. §§ 102/103**

#### **Marshall**

Claims 47-49 and 54-56 also stand rejected under 35 U.S.C. § 102(a) “as being anticipated by, or, in the alternative, under 35 U.S.C. §103(a) as obvious over Marshall et al.” With regard to claim 48, the Examiner has asserted that, while Marshall does not specifically mention the use of “automation” with the disclosed methods for using “aptazyme chips,” automation would have been “immediately envisaged (e.g., anticipated) or in the alternative prima facie obvious” to one of ordinary skill in the art, because chips are “made for automation.” (Office Action, p. 11).

Applicants traverse. As described above and in the Declaration submitted herewith, the Marshall reference is not available as prior art under 35 U.S.C. §102 or under 35 U.S.C. §103 in the instant application. Accordingly, Applicants request that the Examiner withdraw this rejection.

#### **Hesselberth**

Claims 47-49, 56, 58-62 and 65-66 also stand rejected under 35 U.S.C. § 102(a) “as being anticipated by, or, in the alternative, under 35 U.S.C. §103(a) as obvious over Hesselberth et al.” According to the Examiner, Hesselberth does not specifically teach the use of “automation,” as recited by claim 48, but automation would have been “immediately envisaged (e.g., anticipated) or in the alternative prima facie obvious” to one of ordinary skill in the art, because chips are “made for automation.” (Office Action, p. 13).

Applicants traverse. As described above and in the Declaration submitted herewith, the Hesselberth reference is not available as prior art under 35 U.S.C. §102 or under 35 U.S.C. §103

in the instant application. Accordingly, Applicants request that the Examiner withdraw this rejection as well.

#### **IV. Claim rejections under 35 U.S.C. § 103**

##### **Marshall and Cox**

Claims 47-49 and 54-66 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Marshall and Cox, *et al.*, *Biotechnol. Prog.*, vol. 14:845-850 (1998) (“Cox”). Claims 47 and 49 have been rejected in view of the teachings of Marshall, as discussed above. The Examiner has also rejected claim 48 as obvious in view of the combined teachings of Marshall and Cox. According to the Examiner, Cox teaches that *in vitro* selection can be “automated,” and therefore it would have been obvious to one of ordinary skill in the art to combine the methods of Marshall with the automation processes and equipment disclosed by Cox. (Office Action, pp. 15-16).

Applicants traverse. As described above, the Marshall reference is not available as prior art under 35 U.S.C. §102 or under 35 U.S.C. §103. Thus, the Cox reference remains as the sole prior art reference. Cox, however, is insufficient to render the claimed invention obvious. The Cox reference describes methods of automated *in vitro* selection. There is no teaching or suggestion in this reference that would motivate one of ordinary skill in the art to produce aptazyme arrays for detecting an analyte and/or an aptazyme reaction, let alone to automate such methods of detection. Thus, Applicants contend that the methods recited by pending claims 47-49 and 54-66 are novel and nonobvious over the Cox reference. Accordingly, Applicants request that the Examiner withdraw this rejection.

##### **Hesselberth and Cox**

Claims 47, 49, 54, 58, 61-62 and 65-66 also stand rejected under 35 U.S.C. §103(a) as being unpatentable over Hesselberth and Cox. Claims 47 and 49 have been rejected in view of the teachings of Hesselberth, as discussed above. The Examiner has also rejected claim 48 as obvious in view of the combined teachings of Hesselberth and Cox. According to the Examiner, Cox teaches that *in vitro* selection can be “automated,” and therefore it would have been obvious to one of ordinary skill in the art to combine the methods of Hesselberth with the automation processes and equipment disclosed by Cox. (Office Action, p. 19).

Applicants traverse. As described above and in the Declaration submitted herewith, the

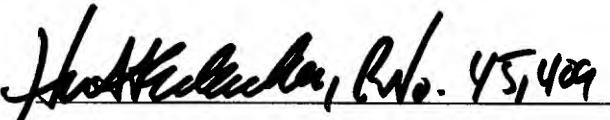
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Hesselberth reference is not available as prior art under 35 U.S.C. §102 or under 35 U.S.C. §103 in the instant application. Thus, the Cox reference remains as the sole prior art reference. As described above, Cox is insufficient to render the claimed invention obvious. Applicants contend that there is no teaching or suggestion in this reference that would motivate one of ordinary skill in the art to produce the aptazyme arrays and methods recited by pending claims 47, 49, 54, 58, 61-62 and 65-66. As such, Applicants request the withdrawal of this rejection.

## CONCLUSION

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

  
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